

REMARKS/ARGUMENTS

Claims 21-35 are pending, claims 25-35 having been withdrawn from consideration. By this Amendment, claim 21 and 25-35 are amended. Support for the amendments to claims 21 and 25-35 can be found, for example, in original claims 21 and 25-35. No new matter is added. In view of the foregoing amendments and following remarks, reconsideration and allowance are respectfully requested.

Withdrawn Claims

For the reasons set forth below, Applicants submit that all pending claims presently subject to examination are in condition for allowance. Because the withdrawn claims depend from, and thus recite all features of, allowable claim 21, rejoinder and allowance of the withdrawn claims are respectfully requested.

Rejection Under 35 U.S.C. §102

The Office Action rejects claims 21 and 22 under 35 U.S.C. §102(b) over U.S. Patent Application Publication No. US 2002/0047058 to Verhoff et al. ("Verhoff"). Applicants respectfully traverse the rejection.

Claim 21 recites "[a] composition, comprising: an extremely poorly water-soluble drug; and a porous silica material; wherein: the composition is obtained by treating a mixture comprising the porous silica material and the extremely poorly water-soluble drug with a supercritical fluid or subcritical fluid of carbon dioxide; the extremely poorly water-soluble drug has a solubility in water at 25 °C of less than 10 µg/mL prior to treatment; and the porous silica material has an average pore diameter of from 1 to 20 nm, a total pore volume of pores having diameters within $\pm 40\%$ of the average pore diameter accounts for at least 60% of a volume of all pores of the porous silica material, and the porous silica material has

an X-ray diffraction pattern including at least one peak at a position of a diffraction angle (2 θ) corresponding to a d value of at least 1 nm" (emphasis added). Verhoff does not disclose or suggest such a composition.

As indicated above, the porous silica material of the composition of claim 21 has an X-ray diffraction pattern including at least one peak at a position of a diffraction angle (2 θ) corresponding to a d value of at least 1 nm. Verhoff does not disclose employing a porous silica material having such an X-ray diffraction pattern. Instead, Verhoff discloses employing the product Nyacol 9950 as a silica material. *See, e.g., Verhoff*, paragraph [0293]. Applicants have attached hereto product information for Bindzil 9950, which is the present trade name for Nyacol 9950.[#] Applicants have carried out experimentation to demonstrate that Nyacol 9950/Bindzil 9950, as employed in Verhoff, does not have the X-ray diffraction pattern required in claim 21.

Applicants experimentation is described in the Declaration Under 37 C.F.R. §1.132 ("Declaration") attached hereto. In particular, samples of the porous silica material employed in Example 1 of the present specification and the silica material employed in Example 1 of Verhoff (Nyacol 9950/Bindzil 9950), were subjected to powder X-ray diffraction analysis. *See Declaration*, paragraph 6. As is evident from the X-ray diffraction patterns in the Declaration, Nyacol 9950/Bindzil 9950, as employed in Verhoff, does not have the X-ray diffraction pattern required in claim 21, while the porous silica material employed in Example 1 of the present specification has the X-ray diffraction pattern required in claim 21. *See Declaration*, paragraph 7. Accordingly, Verhoff does not disclose, either explicitly or inherently, a composition including a porous silica material having such an X-ray diffraction pattern.

[#] Applicants have attached hereto a letter from Eka Chemicals and a partial English-language translation thereof confirming that the product identified as Nyacol 9950 in Verhoff is presently known as Bindzil 9950. Accordingly, the product information relating to Bindzil 9950 accurately describes the characteristics of the Nyacol 9950 used in Verhoff.

The Office Action appears to assert that it would have been obvious to select, e.g., a porous silica material having the X-ray diffraction pattern recited in claim 21, in view of the teachings of Verhoff. See Office Action, pages 4 to 5. As is well-settled, a particular parameter must first be recognized as a result-effective variable before the determination of workable ranges can be said to be an obvious variation. See, e.g., MPEP §2144.05.II.B (citing *In re Antonie*, 195 U.S.P.Q. 6 (C.C.P.A. 1977)). The Office Action fails to identify, in any of the cited references, recognition that the X-ray diffraction pattern recited in claim 21 is a result-effective variable. Absent such recognition, one of ordinary skill in the art would not have had a reasonable expectation of success upon manipulating the silica materials of Verhoff to obtain the porous silica material of claim 21 – one of ordinary skill in the art would not have been motivated to optimize that variable, as asserted by the Office Action.

For the reasons discussed above, a *prima facie* case of obviousness has not been made. However, even if a *prima facie* case were made, such case is rebutted by the results shown in the present specification – "[a] *prima facie* case of obviousness ... is rebuttable by proof that the claimed compounds possess unexpectedly advantageous or superior properties." See MPEP §2144.09 (citing *In re Papesch*, 315 F.2d 381 (C.C.P.A. 1963)). The Examples of the present specification demonstrate that compositions, such as recited in claim 21, provide unexpected, superior dissolution properties relative to known compositions, which are not produced by treating a mixture comprising an extremely poorly water-soluble drug and a porous silica material with a supercritical or subcritical carbon dioxide fluid. See, e.g., present specification, page 29, Table 1; Declaration, paragraph 8. These results are objective evidence of the improvements of the composition of claim 21 over known compositions, and thus these results rebut any suggestion that it would have been obvious to modify the compositions of Verhoff to obtain the composition of claim 21.

While not emphasized in the discussion above, the Office Action asserts that the recitation of "by treating a mixture comprising the very low water-soluble drug and the porous silica material with a supercritical or subcritical carbon dioxide fluid" in claim 21 is product-by-process language that should not be given weight. *See* Office Action, page 4. Applicants submit that the experimental evidence in the present specification clearly demonstrates that the process step recited in claim 21 confers unique properties (e.g., solubility) to the resulting product. The Office Action is requested to provide a basis for ignoring the experimental data in the present specification demonstrating that the properties of products obtained as recited in claim 21 are different from products obtained otherwise.

As explained, claim 21 is not anticipated by Verhoff. Claim 22 depends from claim 21 and, thus, also is not anticipated by Verhoff. Accordingly, reconsideration and withdrawal of the rejection are respectfully requested.

Rejection Under 35 U.S.C. §103

The Office Action rejects claims 21-24 under 35 U.S.C. §103(a) over Verhoff in view of U.S. Patent No. 6,753,330 to Takano et al. ("Takano"). Applicants respectfully traverse the rejection.

For the reasons discussed above, Verhoff fails to disclose or suggest each and every feature of claim 21. Takano does not remedy the deficiencies of Verhoff. Takano is cited for its alleged disclosure of a pharmaceutical solid dispersions including 2-benzyl-5-(4-chlorophenyl)-6-[4-(methylthio)phenyl]-2H-pyridazin-3-one. *See* Office Action, page 7. However, Takano, like Verhoff fails to disclose or suggest a composition including a porous silica material as recited in claim 21. Accordingly, the combination of references fails to disclose or suggest each and every feature of claim 21.

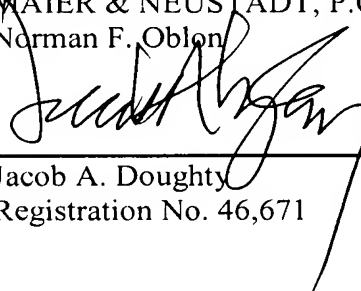
As explained, claim 21 would not have been rendered obvious by Verhoff and Takano. Claims 22-24 depend from claim 21 and, thus, also would not have been rendered obvious by Verhoff and Takano. Accordingly, reconsideration and withdrawal of the rejection are respectfully requested.

Conclusion

For the foregoing reasons, Applicants submit that claims 21-35 are in condition for allowance. Prompt reconsideration and allowance are respectfully requested.

Respectfully submitted,

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Attachments:

Letter from Eka Chemicals and Partial English-Language Translation
Product Information for Bindzil 9950
Declaration Under 37 C.F.R. §1.132